Psychosis

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ABSTRACT

Purpose of Review: Psychosis is a common and functionally disruptive symptom of many psychiatric, neurodevelopmental, neurologic, and medical conditions and an important target of evaluation and treatment in neurologic and psychiatric practice. The purpose of this review is to define psychosis, communicate recent changes to the classification of and criteria for primary psychotic disorders described in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, and summarize current evidence-based approaches to the evaluation and management of primary and secondary psychoses.

Recent Findings: The *DSM-5* classification of and criteria for primary psychotic disorders emphasize that these conditions occur along a spectrum, with schizoid (personality) disorder and schizophrenia defining its mild and severe ends, respectively. Psychosis is also identified as only one of several dimensions of neuropsychiatric disturbance in these disorders, with others encompassing abnormal psychomotor behaviors, negative symptoms, cognitive impairments, and emotional disturbances. This dimensional approach regards hallucinations and delusions as arising from neural systems subserving perception and information processing, thereby aligning the neurobiological framework used to describe and study such symptoms in primary psychotic disorders with those used to study psychosis associated with other neurologic conditions.

Summary: This article provides practicing neurologists with updates on current approaches to the diagnosis, evaluation, and treatment of primary and secondary psychoses.

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INTRODUCTION

Psychosis is a common and functionally disruptive symptom of many psychiatric, neurodevelopmental, neurologic, and medical conditions and an important target of evaluation and treatment in neurologic and psychiatric practice. This article defines psychosis, communicates recent changes to the classification of and criteria for primary psychotic disorders described in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, and summarizes current evidence-based approaches to the evaluation and management of primary and secondary psychoses. The definitions of psychosis used in the *DSM-5* and *International Classification of Diseases, Tenth Revision (ICD-10)* are presented, and hallucinations, delusions, and delu-

sional misidentification syndromes are defined and tabulated. The current classification, updated criteria, and approaches to the evaluation of schizophrenia spectrum and related psychotic disorders, as well as psychoses in neurologic conditions, are reviewed. Practical guidance on the evaluation and treatment of these conditions is drawn from practice guidelines promulgated by the professional societies and other international organizations, supplemented with findings published in more recent meta-analyses and systematic reviews.

Psychosis is the defining feature of schizophrenia spectrum disorders, a common but variable feature of mood and substance use disorders, and a relatively common feature of many developmental, acquired, and degenerative neurologic

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KEY POINT

■ The American Psychiatric Association and the World Health Organization emphasize the presence of hallucinations without insight or delusions in their current definitions of psychosis.

and medical conditions. Across these conditions, psychosis is both a contributor to disability and a barrier to productivity and participation.^{1–4} Psychosis is, therefore, an important target of evaluation and treatment among patients receiving care from neurologists and psychiatrists.

This article also defines psychosis and reviews the essential clinical features of primary psychotic disorders and psychoses secondary to neurologic conditions. The criteria for psychotic disorders included in the *DSM-5*,⁵ which have been revised substantially relative to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*,⁶ are a major focus of this review. The revised diagnostic criteria for secondary psychoses (those due to neurologic or medical conditions, substance use, and medications) also are reviewed briefly and the psychoses associated with common neurologic conditions tabulated. Finally, practical and evidence-based suggestions for the evaluation and treatment of primary and secondary psychotic disorders are presented.

DEFINING PSYCHOSIS

In early editions of the American Psychiatric Association's (APA's) *Diagnostic and Statistical Manual of Mental Disorders (DSM)*,⁷ psychosis was defined broadly as "gross impairment in reality testing" or "loss of ego boundaries" that interferes with the capacity to meet the ordinary demands of life. This approach to defining psychosis emphasized the presence of functional limitations over the symptoms putatively responsible for them⁶ and too often rendered the distinction between psychotic and nonpsychotic mental disorders ambiguous. Concurrently, the *International Classification of Diseases, Ninth Revision (ICD-9)*, published in 1975) employed the then-traditional division between "neurosis" and "psychosis"

in its classification of mental disorders while deliberately making no attempt to define these terms.⁸ As a result, the category of psychotic disorders in the early editions of the *DSM* and in the *ICD-9* were overly inclusive and, with respect to clinical, research, and epidemiologic endeavors, ultimately proved impracticable.^{6,8}

In their current conceptualization of psychosis, both the APA⁵ and the World Health Organization⁸ define psychosis narrowly by requiring the presence of hallucinations (without insight into their pathologic nature), delusions, or both hallucinations without insight and delusions.⁶ In both of these current diagnostic classification systems, impaired reality testing remains central conceptually to psychosis. In contrast to earlier diagnostic classification systems, the current systems^{5,8} operationalize impaired reality testing by identifying the symptoms that provide evidence of such impairment. Delusions (ie, fixed false beliefs), by definition, are evidence of impaired reality testing: delusional beliefs are ones maintained steadfastly even in the face of evidence contradicting them incontrovertibly. Similarly, hallucinations (ie, perceptions occurring in the absence of corresponding external or somatic stimuli) are evidence of impaired reality when the individual experiencing them is unable to recognize the hallucinatory nature of such experiences. Both the current APA⁵ and the World Health Organization⁸ classification systems acknowledge that "formal thought disorder" (ie, disorganized thinking, including illogicality, tangentiality, perseveration, neologism, thought blocking, derailment, or some combination of these disturbances of thought) is one of several commonly co-occurring features of psychotic disorders. The *DSM-5*⁵ allows formal thought disorder to supplant hallucinations and delusions in the diagnosis of a psychotic disorder when it is accompanied by grossly disorganized behavior, catatonia

(for schizophrenia, schizophreniform, brief psychotic, and schizoaffective disorders) and/or negative symptoms (for schizophrenia, schizophreniform, and schizoaffective disorders but not brief psychotic disorder), alone or in combination.⁸ Since mildly disorganized speech is common and diagnostically nonspecific, the degree of thought disorder required to fulfill this *DSM-5* criterion must be of severity sufficient to substantially impair effective communication.

For the purposes of this article, the term *psychosis* refers to the presence of delusions, hallucinations without insight, or both. These symptoms are clearly defined common features of psychosis in both psychiatric disorders and neurologic conditions. They are captured by informal and structured clinical assessments and are reasonably amenable to treatment.

Hallucinations

Hallucination is defined as a sensory perception in the absence of a corresponding external or somatic stimulus and described according to the sensory domain in which it occurs. Hallucinations may occur with or without insight into their hallucinatory nature. The absence of insight into a hallucination defines it as a psychotic symptom, that is, a hallucination for which reality testing is impaired. Hallucinations without insight are contrasted with hallucinations that the individual recognizes as unreal. Examples of hallucinations with preserved insight include the visual hallucinations of migraine aura, sleep transition-related hypnagogic (while falling asleep) and hypnopompic (while waking) hallucinations, and the hallucinated hearing of one's name being called that many psychiatrically and neurologically healthy individuals experience occasionally.

Schneider⁹ described auditory hallucinations involving hearing voices conversing with one another, offering running commentary on one's actions,

and “thought echoes” (hallucinations in which the patient hears his or her thoughts spoken aloud) as “first-rank” symptoms of schizophrenia. The first two of these types of auditory hallucinations have been regarded as so abnormal that their presence alone (in the absence of delusions or other thought, speech, and behavioral disturbances or negative symptoms) was sufficient to warrant a diagnosis of schizophrenia under the criteria of the *DSM-IV-TR*⁶ and its predecessors.

Hallucination is distinguished from illusion (misperception of an actual sensory stimulus) and the other disturbances of perception or experience described in **Table 8-1**.¹⁰ These perceptual phenomena occur in many neuropsychiatric conditions, including primary psychiatric disorders, neurologic disorders, medical illnesses, and substance intoxication and withdrawal states. Some of these perceptual phenomena (eg, illusions, hallucinations, synesthesia, derealization, depersonalization, autoscopy, déjà vu or déjà entendu, jamais vu or jamais entendu) are also reported by neuropsychiatrically healthy individuals. Their occurrence is not necessarily pathologic, especially if they occur with preserved insight, they are not associated with other disturbances of cognition, emotion, or behavior, and they do not compromise personal, social, or occupational function.

Delusions

Delusions are fixed false beliefs; they are based on incorrect (false) inferences about reality external to, or about, oneself and maintained firmly (fixed) despite the presentation of evidence that obviously and incontrovertibly contradicts the belief. **Table 8-2** defines and describes the types of delusions commonly occurring in individuals with primary and secondary psychotic disorders.¹⁰ These delusions are often

KEY POINTS

- Hallucination is defined as a sensory perception in the absence of a corresponding external or somatic stimulus and described according to the sensory domain in which it occurs.
- Hallucinations may occur with or without insight into their hallucinatory nature. The absence of insight into a hallucination defines it as a psychotic symptom, that is, a hallucination for which reality testing is impaired.
- Delusions are fixed false beliefs; they are based on incorrect (false) inferences about reality external to, or about, oneself and maintained firmly (fixed) despite the presentation of evidence that obviously and incontrovertibly contradicts the belief.

TABLE 8-1 Disturbances of Perception and Experience in the Differential Diagnosis of Hallucinations^a

Phenomenon	Description
Hallucination	Sensory perception in the absence of a stimulus; described according to the sensory domain in which it occurs (eg, visual, auditory, tactile, olfactory, gustatory, nociceptive, thermoceptive, proprioceptive, equilibrioceptive); may be unformed (ie, nonspecific sensory perceptions within a sensory domain) or formed (ie, people, objects, voices making comments or commands)
Illusion	Misperception of a sensory stimulus; described according to the sensory domain in which it occurs (eg, visual, auditory, tactile, olfactory, gustatory, nociceptive, thermoceptive, proprioceptive, equilibrioceptive)
Palinopsia	Persistent perception of a visual stimulus after that stimulus is no longer present (ie, an afterimage)
Synesthesia	Perception of a stimulus outside the sensory modality in which that stimulus is presented (eg, hearing colors, tasting sounds) or that adds perceptual features not normally perceived within a sensory modality (eg, black numbers or letters evoking the perception of color)
Derealization	Perceiving/experiencing the external world as unreal
Depersonalization	Perceiving/experiencing oneself as detached from (ie, as if an outside observer of) one's mental processes or body
Autoscopy	Seeing one's body from a position outside the body (ie, out-of-body experience)
Déjà vu	Perceiving/experiencing a novel image or scene as one previously witnessed or experienced
Déjà entendu	Perceiving/experiencing a novel sound as one previously witnessed or experienced
Jamais vu	Perceiving/experiencing a familiar image or scene as unfamiliar
Jamais entendu	Perceiving/experiencing a familiar sound as unfamiliar

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divided into two types: ordinary and bizarre. Ordinary delusions derive from misinterpretation of everyday experiences and, as such, are understandable but not accepted by other members of the person's culture or subculture (ie, are not articles of religious faith). For example, a patient who believes that an unknown group of conspirators is diverting his savings to a terrorist group despite being presented with evidence to the contrary (eg, bank

statements) has an ordinary delusion (more specifically, an ordinary persecutory delusion). Bizarre delusions involve phenomena that are physically impossible or that most people in that person's culture would regard as entirely implausible. The *DSM-IV-TR* provided as an example of bizarre delusion the belief that a stranger removed one's internal organs and replaced them with another person's organs without leaving any wounds or scars.⁶

TABLE 8-2 Delusions Observed Among Patients With Neuropsychiatric Disorders^a

Delusion	Description
Persecutory	Fixed false belief that one is being harmed or that such harm is impending and that the perpetrators of that harm are causing it intentionally; common examples include the belief that one is being followed, tricked, spied on, poisoned or drugged, tormented, ridiculed, cheated, conspired against, or that one's goals are being obstructed
Grandiose	Insightless and unshakable conviction that one possesses special powers, talents, knowledge, or abilities; is famous (or a famous person or character); or holds a special relationship to a famous person or deity
Religious	Any delusion with religious content, especially beliefs that one is God, an angel, a devil, the son or daughter of God, a saint, or otherwise deific (subtypes of grandiose delusions)
Referential	Fixed false belief that remarks, objects, events, or other phenomena are directed at or are about oneself
Thought control	Fixed false belief that one's thoughts, feelings, or behaviors are being controlled by an external force, person, or group
Thought insertion	Delusion that thoughts are being inserted into one's mind ("thoughts are not my own")
Thought withdrawal	Delusion that an outside force, person, or group is removing or extracting one's thoughts
Thought broadcasting	Delusion that one's thoughts are being broadcast to others or can be heard aloud by others
Delusional perception	Linking a normal percept to a bizarre conclusion (eg, seeing the sunrise signifies to the patient that he or she is the messiah)
Mind being read	Delusion that one's mind can be or is being read by another person or group; does not entail "broadcasting" one's thoughts or that one's thoughts can be heard aloud by others; may be a subtype of persecutory (paranoid) delusions
Jealousy	Fixed false belief that a spouse or lover is unfaithful; also referred to as delusion of infidelity
Erotomania	Delusion that one is loved by another person (usually one of higher status)
Theft	Fixed false belief that one's valuables are being stolen, often by an unseen thief; tends to develop in the context of declarative memory impairments (eg, Alzheimer disease)
Phantom intruder	Delusion that a stranger, usually unwanted, is in one's home
Somatic	A delusion that pertains to the appearance or functioning (including smell) of one's body, usually involving the fixed false belief that one's body is abnormal, diseased, or changed in some manner
Parasitosis	Fixed false belief that one is infested with insects, bacteria, mites, lice, fleas, spiders, worms, or other organisms (also known as Ekbom syndrome ^b)
Nihilistic	Delusion that one does not exist or is dead; also described as delusion of negation

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^b Ekbom syndrome should not be confused with Willis-Ekbom disease (ie, restless legs syndrome).

Schneider⁹ described specific types of bizarre delusions as "first-rank" symptoms of schizophrenia. ("First-rank" refers to symptoms that, when present, indicate the presence of a particular diagnosis [in the case of Schneiderian first-rank symptoms, the diagnosis of schizophrenia]). These include delusions of control, including thought control, as well as thought

withdrawal and thought insertion. The presence of bizarre delusions, especially of these types, has long been regarded as so abnormal that their presence alone (in the absence of delusions or other thought, speech, and behavioral disturbances or negative symptoms) was sufficient to warrant a diagnosis of schizophrenia under *DSM-IV-TR* and its predecessors.

KEY POINTS

- Delusions are distinct from confabulation, which refers to the automatic and nondeceitful fabrication of information, usually of an autobiographic or episodic nature, by a patient with concurrent declarative memory impairments and executive dysfunction.
- Although delusional misidentification syndromes occur commonly among patients with psychiatric illnesses, especially primary psychotic disorders, as many as 20% to 40% occur in the context of neurologic conditions affecting the right hemisphere. Accordingly, the presence of these types of delusions should prompt evaluation for potentially treatable or arrestable neurologic conditions.

Delusions are contrasted with overvalued ideas, which are unreasonable beliefs or ideas that are held with strong, but not delusional, conviction. When a false belief involves a value judgment, it may be regarded as delusional only when the judgment made is so extreme that it is not credible. Delusions are distinct from confabulation, which refers to the automatic and nondeceitful fabrication of information, usually of an autobiographical or episodic nature, by a patient with concurrent declarative memory impairments and executive dysfunction.¹¹ Confabulated information (even when fantastic in character) may be firmly believed in the moment that it is offered but is usually soon forgotten and, as such, is false but not fixed and, hence, not delusional.

Delusional misidentification syndromes. Delusional misidentification syndromes (Table 8-3¹⁰) share the theme of doubles (ie, duplication of self, others, or the environment). They are associated with impairments in facial processing and are closely related to and sometimes co-occur with reduplicative paramnesia.^{12,13} Phenomenologically, delusional misidentification syndromes may be divided into two types: delusional hypoidentification (eg, Capgras syndrome) or delusional hyperidentification (eg, Frégoli, intermetamorphosis, subjective doubles syndromes). Although delusional misidentification syndromes occur commonly among patients with psychiatric illnesses, especially primary psychotic disorders, as many as 20% to 40% occur in the context of neurologic conditions affecting the right hemisphere.^{12,13} Accordingly, the presence of these types of delusions should prompt evaluation for potentially treatable or arrestable neurologic conditions.

PRIMARY PSYCHOTIC DISORDERS

A subset of the population with genetic, epigenetic, and developmental risk fac-

tors may, with sufficient exposure to risk-modifying social and environmental factors, be prone to developing persistent psychotic symptoms.^{14–16}

This psychosis proneness-persistence model may explain, at least in part, the development of hallucinations and delusions across the broad range of psychiatric disorders with which they are associated. It also may yield insights into the risk factors for and mechanisms of psychosis associated with neurologic conditions. This model aligns well with the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) framework, within which phenomena such as delusions and hallucinations are studied in relation to the operations of underlying neural systems across the conditions in which they occur, rather than in relation to the categorical psychiatric disorders with which they may be associated.^{17,18}

In this light, it is not surprising that psychosis is listed as a feature of multiple psychiatric disorders presented in the *DSM-5*. Although psychosis is the defining feature of the schizophrenia spectrum disorders (ie, schizophrenia, schizoaffective disorder, delusional disorder, schizophreniform disorder, and brief psychotic disorder), it also occurs in some people with bipolar disorder during either a manic or depressive episode as well as in some individuals during a major depressive episode associated with major depressive disorder. In those conditions, the psychotic symptoms (usually delusions) may be thematically either congruent or incongruent with the prevailing mood. Psychotic symptoms (ie, hallucinations without insight, delusions) may develop during either intoxication or withdrawal from substances and, in some cases, may become chronic sequelae of prior substance use (substance-induced psychotic disorder). When individuals

TABLE 8-3 Examples of Delusional Misidentification and Other Delusions Involving a Belief That the Identity of a Person, Object, or Place Has Been Changed or Replaced^a

Syndrome	Description
Capgras	Delusional belief that a spouse, family member, or other familiar individual has been replaced by an impostor who is physically, but not psychologically, identical to the replaced person
Frégoli	Delusional belief in which the patient believes different people are in fact a single person (usually believed to be a persecutor) who changes appearance or is in disguise
Intermetamorphosis	A variant of the Frégoli syndrome in which the patient believes that familiar people and strangers in the environment swap identities while maintaining their original appearance
Subjective doubles	Delusion that a double of oneself exists (doppelgänger), carrying out independent actions; also known as the subjective Capgras delusion
Clonal pluralization of the self	Delusion that there are multiple physically and psychologically identical copies of oneself
Delusional companions	Fixed false belief that nonliving objects (eg, toys, appliances, cars) are sentient beings
Mirrored self-misidentification	Delusion that one's reflection in a mirror is someone else
Reduplicative paramnesia	Delusion that a familiar person, place, or object has been duplicated
Cotard	Fixed false belief that one or more of one's organs or body parts are missing or no longer exist

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KEY POINT

■ The psychosis proneness-persistence model and Research Domain Criteria approach suggests that the presence of hallucinations or delusions reflects disturbances in the neural systems underlying these symptoms regardless of the categorical psychiatric disorder with which they are associated.

with obsessive-compulsive disorder lack insight into the pathologic nature of their obsessions, their obsessions are described as delusions. The psychosis proneness-persistence model and RDoC approach suggests that the presence of hallucinations or delusions reflects disturbances in the neural systems underlying these symptoms regardless of the categorical psychiatric or neurologic disorder with which they are associated.

A complete review of psychosis as it occurs in each of these conditions is beyond the scope of the present

article. Readers are encouraged to review the relevant sections of the *DSM-5* and to familiarize themselves with the current criteria for these conditions. To help keep readers up-to-date, major changes made to the criteria for psychotic disorders in the transition from the *DSM-IV-TR* to the *DSM-5* are reviewed in this article.

Schizophrenia Spectrum Disorders

The *DSM-5* marks a shift from the presentation of schizophrenia as the archetypal psychotic disorder to its

KEY POINT

■ Disorders along the schizophrenia spectrum differ from one another by the type, number, complexity, severity and duration of the psychotic symptoms and associated features that define them.

consideration as one of several psychotic disorders existing on a spectrum of psychopathology. Disorders along the schizophrenia spectrum differ from one another by the type, number, complexity, severity, and duration of the psychotic symptoms and associated features that define them. Symptoms of schizophrenia spectrum disorders include hallucinations, delusions, disorganized thinking (formal thought disorder, usually inferred from an individual's speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms. The number, complexity, and duration of symptoms required for a given diagnosis increase with movement from the mild to the severe ends of the schizophrenia spectrum.

Consistent with this essentially dimensional approach to the evaluation of psychotic symptoms, the *DSM-5* introduced the Clinician-Rated Dimensions of Psychosis Symptom Severity scale in Section III, "Emerging Measures and Models."^{8,19} This scale is an eight-item measure that rates the severity of each symptom that defines the schizophrenia spectrum disorders (hallucinations, delusions, disorganized speech, abnormal psychomotor behavior, negative symptoms) as well as co-occurring cognitive, depressive, and manic symptoms during the week prior to assessment on a scale from 0 (not present) to 4 (present and severe). Assessment of this constellation of symptoms with these measures is described in the *DSM-5* as useful for characterizing these conditions, predicting important aspects of the illness (eg, cognitive and neurobiological deficits), informing treatment planning and prognosis, and monitoring symptom severity over time. The severity of the disorders in this section of the *DSM-5* may be assessed with this scale, which the APA has made freely available for clinical

use (www.psychiatry.org/File%20Library/Practice/DSM/DSM-5/ClinicianRatedDimensionsOfPsychosisSymptomSeverity.pdf).¹⁹ The provision of this measure is coupled with the request that clinicians and researchers provide further data on the instrument's usefulness in characterizing patient status and improving patient care by submitting feedback at www.dsm5.org/Pages/Feedback-Form.aspx. Given the emerging nature of this measure, the *DSM-5* encourages, but does not require, using the Clinician-Rated Dimensions of Psychosis Symptom Severity scale to specify severity of illness in the schizophrenia spectrum disorders.

Schizotypal (personality) disorder. At the mild end of the schizophrenia spectrum disorders is schizotypal disorder (also known as schizotypal personality disorder). Schizotypal disorder is characterized by social and interpersonal deficits that reduce the capacity for, and produce marked discomfort with, close relationships. These deficits are often accompanied by unusual perceptual experiences (illusions) and cognitive distortions (ideas of reference, suspiciousness or paranoia, odd beliefs, or magical thinking that are held without delusional conviction) similar to, but less severe than, those experienced by people with schizophrenia. As noted by Chemerinski and colleagues,²⁰ schizotypal disorder and schizophrenia feature cognitive, social, and attentional deficits based in neurodevelopmentally mediated temporal and prefrontal cortical pathology. These deficits are milder in people with schizotypal disorder than in those with schizophrenia, possibly as a result of preserved capacity in the schizotypal brain to recruit related brain regions and thereby compensate for dysfunctional areas. Additionally, people with schizotypal disorder appear to be less vulnerable to psychosis as a result of the preservation of protective factors

against the psychotogenic effects of subcortical dopaminergic hyperactivity. Although the criteria for schizotypal disorder have not changed substantively between the *DSM-IV-TR* and *DSM-5*, the presentation of this condition as both a schizophrenia spectrum disorder and a personality disorder is a noteworthy change in its classification.

Delusional disorder. Delusional disorder encompasses a broader range of the spectrum of psychosis severity in the *DSM-5* than in the prior edition of this manual. In both the *DSM-IV-TR* and *DSM-5*, this diagnosis requires the presence of one or more delusions lasting at least 1 month in the absence of prominent hallucinations (**Case 8-1**). If present, hallucinations must be related to the delusional theme (eg, tactile hallucinations of bugs on the skin in a patient with delusions of parasitosis). In the *DSM-IV-TR*, bizarre delusions exceeded the criteria for delusional disorder and were sufficient grounds for a diagnosis of schizophrenia (even in the absence of hallucinations, disorganized thought or behavior, catatonia, or negative symptoms).⁶ In the *DSM-5*, however, allowance of Schneiderian first-rank symptoms to suffice for the diagnosis of schizophrenia has been eliminated. As a result, the presence of either ordinary or bizarre delusions (or both) is now consistent with a diagnosis of delusional disorder, although the presence of bizarre content is used as a specifier in this diagnosis.

Brief psychotic disorder. This diagnosis is defined by the presence of delusions, hallucinations, formal thought disorder (ie, disorganized speech), or abnormal psychomotor behavior (grossly disorganized or catatonic behavior), not better explained by another mental disorder, substance use disorder, or medical condition, lasting at least 1 day but less than 1

month, with eventual full return to premorbid function. Negative symptoms are not among the diagnostic criteria for this condition. As in the *DSM-IV-TR*, current specifiers for brief psychotic disorder include the condition's relationship to marked stressors (which, if present, define brief reactive psychosis) or postpartum onset (during pregnancy or within 4 weeks postpartum). The *DSM-5* adds a specifier for the presence of catatonia, as well as a coding note directing the use of the additional 293.89 code (catatonia associated with brief psychotic disorder) to indicate this comorbidity.

Schizophreniform disorder. Schizophreniform disorder represents a point on the spectrum between brief psychotic disorder and schizophrenia. Analogous to changes made to the criteria for schizophrenia, this condition is defined by the presence of two or more psychotic and related symptoms (delusions, hallucinations, disorganized speech reflecting formal thought disorder, abnormal psychomotor behavior such as grossly disorganized or catatonic behavior, negative symptoms)—at least one of which must be delusions, hallucinations, or disorganized speech—lasting at least 1 month but less than 6 months. The *DSM-5*, in contrast to the *DSM-IV-TR*, permits making a provisional diagnosis of schizophreniform disorder when a diagnosis must be made before the end of this time period (without waiting for possible recovery). It also clarifies the exclusion of schizoaffective disorder, major depressive disorder, and bipolar disorder by specifying that no major depressive or manic symptoms may occur with active-phase psychotic symptoms or, if such symptoms have been present, that they have been present for a minority of the total active and residual phases of the illness. As with brief psychotic disorder, an additional

KEY POINT

■ Although the criteria for schizotypal disorder have not changed substantively between the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* and the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, the presentation of this condition as both a schizophrenia spectrum disorder and a personality disorder is a noteworthy change in its classification.

KEY POINT

- The *DSM-5* eliminates the presence of first-rank hallucinations or delusions as grounds for reducing the number of symptoms required for the diagnosis of schizophrenia.

Case 8-1

A 19-year-old previously healthy man was brought in by his parents for evaluation of paranoid ideation. The parents reported that the patient had always been a loner, worked from home as a computer programmer, and spent most of his leisure time in his room browsing the Internet, watching detective shows on television, and listening to a police scanner. A little over 1 month prior to presentation, he began refusing to leave his room, keeping the curtains drawn constantly, and taking copious notes about the comings and goings of his neighbors. After a week of these new behaviors, his parents asked him to explain the changes to his routine. He told them that a black sedan had begun parking across the street from their home each evening and departing early each morning, leading him to conclude that he was the subject of surveillance by the Federal Bureau of Investigation. When his parents informed him that the car was recently purchased by their longtime next-door neighbor and family acquaintance, he then concluded that the neighbor was the federal agent surveilling him. Despite repeated attempts to convince him otherwise, including a conversation with the neighbor, who explained his recent purchase of a luxury car to ease his long daily commutes, the patient's paranoid beliefs remained unchanged. Physical and neurologic examinations were normal, and mental status examination was remarkable only for the patient's delusion. Serum laboratory studies, urine toxicology, and MRI of the brain were normal.

Comment. The patient presented with a nonbizarre delusion as his sole symptom. The presence of this type of delusion for more than 1 month in the absence of prominent hallucinations, when not better explained by a known psychotic disorder or mood disorder with psychotic features and not attributable to the physiologic effects of a substance or another medical condition, is consistent with a provisional diagnosis of delusional disorder (297.1), current severity of delusions: 4 (present and severe).

specifier and related coding note have been added to indicate the presence of comorbid catatonia.

Schizophrenia. The *DSM-5* includes substantive changes to the diagnostic criteria for schizophrenia. The core criteria continue to require the presence of two or more psychotic and related symptoms (delusions, hallucinations, disorganized speech reflecting formal thought disorder, abnormal psychomotor behavior such as grossly disorganized or catatonic behavior, negative symptoms)—at least one of which must be delusions, hallucinations, or disorganized speech—that have been present for at least 6 months (including 1 month, or less if treated successfully, of active psychotic and related symptoms). These symptoms also

must be associated with impaired functioning in one or more major life areas such as self-care, work, interpersonal relations, or academics.

The *DSM-IV-TR* permitted diagnosing schizophrenia when first-rank delusions or auditory hallucinations occurred in the absence of other symptoms. However, first-rank symptoms are not specific to schizophrenia and may occur in manic and depressive episodes with psychotic features, temporal lobe epilepsy, dissociative identity disorder, and other psychiatric conditions.²¹ Accordingly, the *DSM-5* eliminates the presence of first-rank hallucinations or delusions as grounds for reducing the number of symptoms required for the diagnosis of schizophrenia. This change is coordinated with the *DSM-5* revised

criteria for delusional disorder such that patients presenting only with bizarre delusions, and thereby failing to meet criteria for schizophrenia, can now be diagnosed with delusional disorder. As with schizophreniform disorder, clarification of the exclusion of schizoaffective disorder, major depressive disorder, and bipolar disorder is offered, and an additional specifier and related coding note have been added to indicate the presence of comorbid catatonia.

In contrast to prior editions of the *DSM*, schizophrenia subtypes have been eliminated in *DSM-5*. These subtypes (paranoid, disorganized, catatonic, undifferentiated, residual) were defined previously by the predominant symptom at the time of a given evaluation. However, the validity of these subtypes was controversial given their longitudinal instability, overlapping features, and failure to consistently predict outcomes.²² Recognizing these problems and the waning use of schizophrenia subtypes in clinical and research contexts,²³ the *DSM-5* eliminates schizophrenia subtyping in favor of characterizing the features of schizophrenia using the Clinician-Rated Dimensions of Psychosis Symptom Severity scale.

Schizoaffective disorder. Defining schizoaffective disorder has presented challenges to the psychiatric research community.²⁴ Some investigators regard it as variant of schizophrenia in which mood symptoms are unusually prominent but not unusual in type. Others describe it as a mood disorder in which mood episode-related psychotic symptoms do not fully remit. Still others view it as the simple co-occurrence of two relatively common but etiologically distinct psychiatric illness types, schizophrenia and a mood disorder. The problem of schizoaffective disorder remains unresolved in the *DSM-5*, although

criteria are revised in a manner that is likely to reduce the frequency with which it is diagnosed.

As in the *DSM-IV-TR*, the current diagnostic criteria for schizoaffective disorder require an uninterrupted period of illness during which a major mood episode occurs concurrently with a disturbance meeting Criterion A for schizophrenia (two or more of the following: delusions, hallucinations, disorganized speech reflecting formal thought disorder, abnormal psychomotor behavior, negative symptoms, at least one of which is delusions, hallucinations, or disorganized speech). Over the lifetime of the illness, delusions or hallucinations also must occur for at least 2 weeks in the absence of either a manic or depressive episode. This requirement of a 2-week (or longer) episode of psychosis in the absence of mood symptoms distinguishes schizoaffective disorder from either bipolar or depressive disorders with psychotic features, in which psychotic symptoms occur only during mood episodes. Course specifiers for bipolar or depressive subtypes of schizoaffective disorder and a new specifier for catatonic features are presented in the current criteria.

In contrast to the *DSM-IV-TR*, however, the *DSM-5* requires the presence of symptoms meeting criteria for manic and/or depressive episodes for the majority (not merely a substantial portion) of the total duration of the illness. This criterion requires assessment of mood symptoms over the entire course of a psychotic illness rather than merely the current period of illness; if mood symptoms are present only for a relatively brief period (eg, during only 1 year of a 4-year psychotic illness), then a diagnosis of schizophrenia is made instead of a diagnosis of schizoaffective disorder. The information requirements needed to confidently establish a diagnosis of schizoaffective

KEY POINTS

- In contrast to prior editions of the *DSM*, schizophrenia subtypes have been eliminated in the *DSM-5*.
- The *DSM-5* eliminates schizophrenia subtyping in favor of characterizing the features of schizophrenia using the Clinician-Rated Dimensions of Psychosis Symptom Severity scale.

KEY POINT

■ New in the *DSM-5* is the instruction to use the “unspecified schizophrenia spectrum and other psychotic disorder” diagnosis in circumstances in which the clinician chooses not to specify the reason that the criteria are not met for another schizophrenia spectrum or psychotic disorder.

disorder necessitate a fully informed longitudinal perspective on the totality of a patient’s symptoms that often will not be arrived at easily, if at all, in many clinical practices.

Other specified schizophrenia and other psychotic disorders. The *DSM-5* introduces this subcategory to provide for the diagnosis of four conditions involving psychotic symptoms that do not meet full criteria for any of the schizophrenia spectrum disorders but nonetheless are issues of clinical concern. Below are examples of clinical presentations to which the “other specified” designation applies.

- *Persistent auditory hallucinations*, denoting the persistent presence of auditory hallucinations occurring in the absence of other psychotic features.
- *Delusions with significant overlapping mood episodes*, which is most appropriately used when a patient otherwise meeting criteria for delusional disorder also experiences overlapping mood episodes for a substantial portion of the delusional disturbance.
- *Attenuated psychosis syndrome*, which describes a condition in which psychotic-like symptoms are present but are less severe and more transient than in schizophrenia, and for which insight is relatively maintained.
- *Delusional symptoms in a partner of individual with delusional disorder* (formerly named shared psychotic disorder, also known as folie à deux), a rare condition in which delusions develop in an individual who is involved in a close relationship with an individual with prominent delusions. The previously unaffected partner’s delusions take on the content of the dominant partner’s delusions.

Unspecified schizophrenia spectrum and other psychotic disorder. The *DSM-5* replaces “psychotic disorder not otherwise specified” with “unspecified schizophrenia spectrum and other psychotic disorder.” As in the *DSM-IV-TR*, this diagnosis applies to presentations in which functionally disabling or subjectively distressing symptoms characteristic of schizophrenia spectrum and other psychotic disorders predominate but do not meet full criteria for another condition in this category. It also applies to presentations about which insufficient information exists to make a more specific diagnosis. New in the *DSM-5* is the instruction to use the “unspecified schizophrenia spectrum and other psychotic disorder” diagnosis in circumstances in which the clinician chooses not to specify the reason that the criteria are not met for another schizophrenia spectrum or psychotic disorder. The practical usefulness of this diagnosis is not established.

SECONDARY PSYCHOTIC DISORDERS

The *DSM-5* notes the common co-occurrence of psychotic symptoms (ie, hallucinations without insight, delusions) in people with neurocognitive disorders due to Alzheimer disease, Parkinson disease, diffuse Lewy body disease, frontotemporal lobar degeneration, Huntington disease, prion disease, cerebrovascular disease, traumatic brain injury, HIV, and substances/medications, among others. When psychotic symptoms develop in association with cognitive impairments due to these conditions, the *DSM-5* suggests qualifying the neurocognitive disorder diagnosis with the specifier “with behavioral disturbance (psychosis)” rather than offering a concurrent schizophrenia spectrum disorder diagnosis. When hallucinations or delusions predominate the clinical presentation, are not better

explained by another mental disorder, are not merely symptoms of a delirium, are functionally impairing or distressing, and when there is evidence that their occurrence is pathophysiologically linked to either a neurologic or medical condition or substance abuse or medication, then a diagnosis of “psychotic disorder due to another medical condition” or “substance/medication-induced psychotic disorder,” respectively, may be made.

A detailed review of the clinical features of psychosis associated with neurologic conditions is beyond the scope of this review, as the literature describing the phenomenology, epidemiology, and putative neurobiology of hallucinations and delusions associated with neurologic disorders has expanded rapidly over the last 2 decades. As a brief

review, **Table 8-4**^{25,26} summarizes and comments on the psychotic symptoms associated with more than a dozen neurologic conditions and their possible anatomic correlates.

EVALUATION AND MANAGEMENT

Useful direction for the evaluation and management of patients with schizophrenia spectrum and related disorders,²⁷ as well as other psychiatric and neurologic conditions in which psychotic symptoms developed, is found in the APA Clinical Practice Guidelines (psychiatryonline.org/guidelines).²⁸ The American Academy of Neurology (AAN) practice parameters and evidence-based guidelines (www.aan.com/Guidelines) may also be useful for clinicians evaluating and managing patients with secondary

TABLE 8-4 Examples of Neurologic Conditions Associated With Psychosis^{a,b}

Condition	Typical Symptoms ^c	Anatomic Correlations	Comment
Adrenoleukodystrophy	Delusions including paranoia Hallucinations including auditory	Temporoparietal white matter	This is a rare condition and few patients with it experience psychosis; nonetheless, psychosis may be a presenting feature of this disorder
Alzheimer disease	Delusions, including misidentification syndromes, are the most common symptoms Hallucinations (visual more than auditory more than olfactory)	Medial temporal and temporoparietal areas, basal forebrain cholinergic nuclei leading to cortical cholinergic deficit	Increasingly common as illness severity and duration increase Misidentification syndromes may be an extension of a variety of cognitive impairments such as anosognosia, visuospatial dysfunction, or memory impairment, but the quality of such problems may, in some cases, become delusional
Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis ²⁶	Delusions, hallucinations, catatonia	Frontotemporal hypermetabolism and occipital hypometabolism on positron emission tomography (PET)	Psychosis occurs in the context of associated confusional state, decreased level of consciousness, catatonia, behavioral changes, dyskinesia, and dysautonomia

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TABLE 8-4 Examples of Neurologic Conditions Associated With Psychosis^{a,b} *Continued from page 727*

Condition	Typical Symptoms ^c	Anatomic Correlations	Comment
Cortical or subcortical stroke	Delusions Hallucinations (visual more than auditory) including release hallucinations	Temporoparietal cortex or subcortical gray matter	Psychosis appears to be more common with right temporo-parieto-occipital junction lesions; however, left-sided lesions also producing Wernicke aphasia may be associated with psychosis Risk of psychosis following stroke may be increased by cerebral atrophy or ischemic white matter disease
Diffuse Lewy body disease	Hallucinations, predominantly visual, but auditory, olfactory, and tactile may occur Delusions	Anterior frontal and temporal cortices including amygdalae, basal forebrain cholinergic nuclei leading to cortical cholinergic deficit	Visual hallucinations may be a prominent early feature, in contrast to Alzheimer disease (in which such features are late and less common than delusions) and Parkinson disease (in which such features are late or related to dopaminergic therapy)
Dopaminomimetic therapy for Parkinson disease and Parkinson plus syndromes	Paranoid ideation, paranoid delusions Visual hallucinations	Mesolimbic dopaminergic target sites	A common problem following administration of these agents particularly among patients with relatively advanced disease; note, however, that psychotic symptoms may develop as an intrinsic feature of Parkinson disease and other Lewy body diseases
Epilepsy	Delusions Hallucinations Schizophreniform psychosis	Medial temporal lobe and associated paralimbic and neocortical network elements	Psychosis appears to be more common with left-sided foci Although psychosis is typically an interictal (or subacute postictal) problem, partial complex status and absence status may be mistaken for psychosis
Fahr disease (idiopathic basal ganglia calcification)	Delusions including paranoid delusions Hallucinations including auditory (sometimes musical) and complex visual illusions Thought disorder Schizophreniform psychosis	Caudate nucleus, especially medial aspect of the head of this nucleus	The relationship between basal ganglia calcification (either idiopathic or secondary) is contentious; while paranoia is more common in patients with basal ganglia calcifications, the presence of calcifications is not more frequent than expected in the population of patients with neuropsychiatric disorders

Continued on page 729

TABLE 8-4 Examples of Neurologic Conditions Associated With Psychosis^{a,b} *Continued from page 728*

Condition	Typical Symptoms ^c	Anatomic Correlations	Comment
Frontotemporal lobar degeneration	Delusions	Disproportionate temporal lobe atrophy (temporal lobe variant)	Psychosis in frontotemporal lobar degeneration is associated with TDP-43 type B and FUS pathologies, and higher with genetic mutations of <i>C9ORF72</i> and <i>GRN</i> ; in some series, asymmetric right-sided involvement is associated with delusions
Ischemic white matter disease	Delusions	Frontal white matter of the frontal subcortical circuits or temporoparieto-occipital areas involving auditory or visual pathways	More common with extensive and bilateral disease than with single lesions
Hexosaminidase deficiencies (A: Tay-Sachs disease, or A and B: Sandhoff disease)	Schizophreniform psychosis	Subcortical gray matter and cerebellum, as well as a lesser degree of diffuse cerebral involvement	In adult-onset Tay-Sachs disease, psychosis occurs commonly and may be the presenting feature of this condition
Huntington disease	Hallucinations Delusions Schizophreniform psychosis	Caudate nucleus, especially medial aspect of the head of this nucleus	Psychiatric symptoms may precede onset of motor symptoms, but delusions are more commonly a late feature of the disease; delusions and hallucinations commonly co-occur with depression
Limbic encephalitis (paraneoplastic or autoimmune) ²⁶	Delusion, hallucinations	Limbic structures	Intracellular, onconeural antigens (Hu, CRMP-5, Ri, Yo, Ma2) Intracellular, synaptic antigens (GAD, amphiphysin) Cell surface or synaptic receptors (NMDAR, AMPAR, GABA-B R, LGI1, Caspr2, GlyR)
Metachromatic leukodystrophy	Schizophreniform psychosis	Temporolimbic, frontal, and periventricular white matter	Psychosis is a rare feature of this rare disease
Multiple sclerosis	Hallucinations Thought disorder Delusions	Temporoparietal white matter, frontal white matter, or subcortical white matter	Tends to be a relatively late feature of the disease and is related to increased plaque burden in the areas noted May wax and wane with acute lesion formation, inflammation, and resolution in the relevant areas
Neoplasm	Schizophreniform psychosis	Pituitary or suprasellar area, temporal lobe, limbic-paralimbic regions, diencephalon and tissue surrounding the third ventricle, and frontal lobes	May result from a range of tumors; laterality of tumor location and onset of psychosis does not appear as highly correlated as in some of the other conditions listed here Neurodevelopmental tumors (dermoid tumors, epidermoid tumors, and teratomas) appear to confer higher risk of psychosis

Continued on page 730

TABLE 8-4 Examples of Neurologic Conditions Associated With Psychosis^{a,b} *Continued from page 729*

Condition	Typical Symptoms ^c	Anatomic Correlations	Comment
Parkinson disease	Delusions (paranoid) Hallucinations including formed visual hallucinations	Cortical atrophy, basal forebrain cholinergic atrophy resulting in cortical cholinergic deficit	May be an idiopathic manifestation of late disease; associated with advanced age, dementia or a premorbid history of schizophrenia, and relatively high doses of prodopaminergic medications In patients with psychosis early in the disease or with relatively more minor motor symptoms, consider diffuse Lewy body disease as an alternative etiology In these patients, psychotic symptoms may result from dopaminomimetic medications used to treat motor symptoms
Traumatic brain injury	Schizophreniform psychosis Delusions, paranoia, and visual hallucinations	Temporal or frontal lobes Right hemisphere, including temporoparietal and frontal areas	More commonly associated with left-sided temporal lobe injuries; frontal lesions may be less strongly associated with psychosis due to traumatic brain injury Psychotic symptoms due to right hemispheric injury may be more specific (eg, delusions alone) and therefore less "schizophreniform"
Wilson disease (hepatolenticular degeneration)	Hallucinations Delusions Schizophreniform psychosis	Putamen and possibly also globus pallidus, thalamus, cortex, and intervening white matter	Psychosis may be the presenting sign of Wilson disease The association between putaminal copper deposition and psychosis is contentious, but may be understood as being similar to the frontal-subcortical and limbic-subcortical aberrations of schizophrenia

TDP-43 = TAR DNA binding protein 43 kDa; FUS = fused in sarcoma; CRMP-5 = collapsin response mediator protein-5; Ma2 = paraneoplastic Ma antigen 2; GAD = glutamate decarboxylase 1; AMPAR = α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; GABA-B = γ -aminobutyric acid; LGI1 = leucine-rich, glioma inactivated 1; Caspr2 = contactin associated protein-like 2; FlyR = glycine receptor.

^a Adapted with permission from McAllister TW, Arciniegas DB, Cambridge University Press.²⁵ © 2013 Cambridge University Press.

^b Childhood disorders, and, in particular, mental retardation, pervasive developmental disorder, autism, and other congenital conditions may also carry an increased risk of psychosis, but are not included here.

^c Schizophreniform psychosis connotes a condition in which hallucinations, delusions, and thought disorder occurs simultaneously and in a fashion that closely resembles schizophrenia. When delusions, hallucinations, or thought disorder may arise as independent symptoms, these terms are listed separately.

psychoses.²⁹ More recent guidelines on these topics, including those promulgated in 2013 by the Scottish Intercollegiate Guidelines Network (SIGN),³⁰ are freely available from the National Guideline Clearinghouse

(www.guideline.gov).³¹ With regard to the application of guidelines to clinical decision making, the Agency for Healthcare Research and Quality recommends using guidelines published within 5 years of the time at which they are

used (www.guideline.gov/about/inclusion-criteria.aspx). Thus, clinicians evaluating and developing treatment plans for patients with primary or secondary psychoses are encouraged to access guidelines in the National Guideline Clearinghouse repository and similar resources,^{32–34} to integrate the guidance they offer with that presented in relevant professional society guidelines (especially when those guidelines are more than 5 years old), and to supplement all guidelines with findings presented in subsequently published meta-analyses and systematic reviews.

Evaluation

Central to all of the presently available guidelines on the evaluation and management of patients with psychosis is the need to identify the cause of psychotic symptoms (in order of priority: delirium, including delirium due to substance intoxication/withdrawal; secondary psychoses of neurologic, medical, and substance use disorders; mood disorders with psychotic features; schizophrenia spectrum disorders; and other psychotic disorders) through comprehensive neuropsychiatric assessment. Patients should be involved in psychiatric, neurologic, and general medical history taking to the extent that their clinical status allows, and, whenever possible, collateral and corroborative history should be obtained from family members or others knowledgeable about the patient and from medical records. Evaluation for potentially causative or contributory medications (eg, prodopaminergic or anticholinergic agents) and substance use disorders is essential.²⁷ Vital signs and body mass index measurements, physical, neurologic, and mental status examinations, and evaluation for substance use should be performed routinely.²⁷ When the history or examination findings suggest that psychotic symptoms may be the product

of a subacute or chronic neurologic condition, neuroimaging (CT or MRI) and EEG may be diagnostically informative.²⁷ When the history or examination findings suggest the presence of either delirium or another nonpsychiatric cause of psychotic symptoms, relevant serum, urine, and CSF studies should be performed.

With regard to evaluation of the psychosis specifically, patient interview and observation using the Brief Psychiatric Rating Scale (BPRS)³⁵ or Positive and Negative Syndrome Scale (PANSS)³⁶ as well as interview of a knowledgeable informant using one of the several versions of the Neuropsychiatric Inventory (NPI)³⁷ (npitest.net), may be useful. Evaluation for manic and depressive episodes (current and lifetime) anchored to *DSM-5* criteria should be performed, as strict adherence to these criteria is required to distinguish between schizophrenia mood disorders with psychotic features and schizoaffective disorder. The *DSM-5* encourages use of the Clinician-Rated Dimensions of Psychosis Symptom Severity scale to rate the severity of both manic and depressive symptoms associated with schizophrenia spectrum and other psychotic disorders.¹⁹ Cognitive and functional assessments, to the extent the patient is able to participate effectively in them, also guide diagnosis and treatment planning. The *DSM-5* directs clinicians to interpret measures using normative data for age and for socioeconomic status; as few measures provide socioeconomic status-adjusted norms, normative data for education may serve as the closest proxy for this adjustment. The Clinician-Rated Dimensions of Psychosis Symptom Severity scale rates the severity of cognitive impairment in increments of standard deviations (SD) below the mean for age and socioeconomic status (0: no impairment; 1: equivocal, between 0 and 0.5 SD; 2: mild, –0.5 to –1 SD; 3:

KEY POINTS

- When evaluating and developing treatment plans for patients with primary or secondary psychoses, clinicians are encouraged to access guidelines in the National Guideline Clearinghouse repository and similar resources to integrate the guidance they offer with that presented in relevant professional societies' guidelines and to supplement all guidelines with findings presented in subsequently published meta-analyses and systematic reviews.
- The *DSM-5* directs clinicians to interpret measures using normative data for age and for socioeconomic status; as few measures provide socioeconomic status-adjusted norms, normative data for education may serve as the closest proxy for this adjustment.

KEY POINTS

- Systematic reviews and meta-analyses demonstrate that typical (first-generation) and atypical (second-generation) antipsychotics are similar with respect to their beneficial effects on the frequency and severity of hallucinations and delusions.
- Meta-analyses suggest that repetitive transcranial magnetic stimulation over the left temporoparietal region (in the area of T3-P3 in the International 10-20 System of Electrode Placement) is an effective treatment for the auditory verbal hallucinations that are refractory to treatment with antipsychotics.
- Acetylcholinesterase inhibitors, adjunctively or alternatively, may reduce psychosis in patients with Alzheimer disease, Parkinson disease dementia, diffuse Lewy body disease, and, to a lesser extent, schizophrenia and related conditions.
- Evidence of benefit from antipsychotic treatment of psychotic symptoms is mixed in patients with psychosis associated with Alzheimer disease, modest in Parkinson disease (for which clozapine and quetiapine are the preferred agents for psychosis that persists despite stepwise reductions in prodopaminergic medications), and limited for most other neurologic conditions.

moderate, -1 to -2 SD; 4: severe, less than -2 SD).¹⁹ Neuropsychological and occupational therapy consultations contribute usefully to cognitive and functional assessments and should be performed when feasible.

Treatment

Systematic reviews and meta-analyses demonstrate that typical (first-generation) and atypical (second-generation) antipsychotics are similar with respect to their beneficial effects on the frequency and severity of hallucinations and delusions.^{38,39} Clozapine is particularly effective in treatment-resistant populations and reduces suicide risk.^{39,40} Among patients with schizophrenia, atypical antipsychotics improve cognition⁴¹ and life satisfaction⁴² and may modestly contribute to improvements in functional status.⁴³ Meta-analyses suggest that repetitive transcranial magnetic stimulation (rTMS) over the left temporoparietal region (in the area of T3-P3 in the International 10-20 System of Electrode Placement) is an effective treatment for the auditory verbal hallucinations that are refractory to treatment with antipsychotics.⁴⁴ However, rTMS does not appear to be an effective treatment for other symptoms of schizophrenia.⁴⁵

Acetylcholinesterase inhibitors, adjunctively or alternatively, may reduce psychosis in patients with Alzheimer disease,⁴⁶ Parkinson disease dementia,⁴⁷ diffuse Lewy body disease,⁴⁸ and, to a lesser extent, schizophrenia and related conditions.⁴⁹ However, antipsychotics remain commonly used to treat psychotic symptoms associated with neurologic disorders. Evidence of benefit from antipsychotic treatment of psychotic symptoms is mixed in patients with psychosis associated with Alzheimer disease,^{50,51} modest in Parkinson disease (for which clozapine and quetiapine are the preferred agents

for psychosis that persists despite stepwise reductions in prodopaminergic medications),⁵² and limited for most other neurologic conditions. While acknowledging the limits of the evidence base for the treatment of psychosis associated with neurologic conditions, individual patients experiencing secondary psychosis may benefit, nonetheless, from judicious administration of antipsychotic medications, especially when other medications and nonpharmacologic interventions do not provide adequate relief from psychotic symptoms.^{53,54}

Whether used to treat primary or secondary psychoses, antipsychotic treatment-related pretreatment evaluation of weight; metabolic status; cardiac, sexual, and neurologic (especially motor) function; and hematologic health as well as periodic monitoring for changes in these areas during treatment is recommended.²⁷ The specific risks and parameters requiring monitoring differ between antipsychotics.^{38,55} Readers are encouraged to review the manufacturer's product information for any specific medication prescribed as well as the recommendations on antipsychotic medication safety monitoring offered in the report of the Mount Sinai Conference on the Pharmacotherapy of Schizophrenia,⁵⁶ and by the 2013 Scottish Intercollegiate Guidelines Network (SIGN).³⁰ Among elderly patients with dementia and psychosis, the benefits of antipsychotic treatment must be balanced against the risk of serious adverse events. Informed consent requires acknowledgement of the 1.5 to 1.8 times increased mortality associated with antipsychotic treatment in elderly patients with dementia, the risk of which appears similar for both the typical and atypical antipsychotics⁵⁴ (www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124830.htm).⁵⁷

Psychosocial interventions also are essential elements of the treatment for patients with primary and secondary psychoses, especially during the stable phase of illness.²⁷ These interventions include patient and family education, cognitive behaviorally oriented therapies, family interventions, assertive community treatment, social skills training, and supported employment. Additional non-pharmacologic interventions that may reduce contributors to psychotic symptoms, especially among patients with dementia-associated psychosis, include improving sensory function (eg, hearing aids, eyeglasses), identifying environmental antecedents to perceptual or cognitive misinterpretations, and stimulus controls that circumvent misinterpretations. Caregiver and family support also should be provided concurrently with patient-oriented therapies.⁵⁸

CONCLUSION

Psychosis is a common symptom of many psychiatric, neurodevelopmental, neurologic, and medical conditions and is an important target of evaluation and treatment in neurologic and psychiatric practice. The *DSM-5* classification of and criteria for primary psychotic disorders emphasize that these conditions occur along a spectrum, with schizoid (personality) disorder and schizophrenia defining its mild and severe ends, respectively. Psychosis is also identified as only one of several dimensions of neuropsychiatric disturbance in these disorders, with others encompassing abnormal psychomotor behaviors, negative symptoms, cognitive impairments, and emotional disturbances. This dimensional approach regards hallucinations and delusions as arising from neural systems subserving perception and information processing, thereby aligning the neurobiological framework used to describe and study such symptoms in primary psychotic disorders with

those used to study psychosis associated with other neurologic conditions.

Comprehensive neuropsychiatric assessment is a prerequisite to the treatment of psychotic symptoms, and it prioritizes identification of medical, substance-related, and neurologic causes of psychosis over their attribution to psychiatric conditions. The use of structured clinical interviews of patients and knowledgeable informants to clarify the character of psychosis and associated symptoms is recommended in guidelines promulgated by the APA and similar professional societies. Data yielded by such interviews establishes a baseline for monitoring disease progression and against which the effects of treatment can be compared. Those treatments include pharmacotherapies and psychosocial interventions, the specific elements of which should follow up-to-date guidelines and findings presented in published meta-analyses and systematic reviews.

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USEFUL WEBSITES

American Psychiatric Association. The American Psychiatric Association (APA) has developed the Clinician-Rated Dimensions of Psychosis Symptom Severity scale, an eight-item measure that rates the severity of each symptom that defines the schizophrenia spectrum disorders as well as co-occurring cognitive, depressive, and manic symptoms during the week prior to assessment.

www.psychiatry.org/File%20Library/Practice/DSM/DSM-5/ClinicianRatedDimensionsOfPsychosisSymptomSeverity.pdf

KEY POINTS

- While acknowledging the limits of the evidence base for the treatment of psychosis associated with neurologic conditions, individual patients experiencing secondary psychosis may benefit, nonetheless, from judicious administration of antipsychotic medications, especially when other medications and nonpharmacologic interventions do not provide adequate relief from psychotic symptoms.
- Among elderly patients with dementia and psychosis, the benefits of antipsychotic treatment must be balanced against the risk of serious adverse events and discussion of both must be included in the informed consent process prior to initiating treatment with antipsychotic medications.
- Readers are encouraged to review the manufacturer's product information for any specific medication prescribed as well as the recommendations on antipsychotic medication safety monitoring offered in the report of the Mount Sinai Conference on the Pharmacotherapy of Schizophrenia and by the 2013 Scottish Intercollegiate Guidelines Network.

KEY POINT

■ Psychosocial interventions also are essential elements of the treatment for patients with primary and secondary psychoses, especially during the stable phase of illness.

The APA offers the Clinician-Rated Dimensions of Psychosis Symptom Severity scale without cost for clinical use, but requests that clinicians and researchers provide data on the instrument's usefulness by submitting feedback at the website below.

dsm5.org/Pages/Feedback-Form.aspx

The APA also offers practice guidelines that provide evidence-based recommendations for the assessment and treatment of psychiatric disorders.

psychiatryonline.org/guidelines

Agency for Healthcare Research and Quality. The Agency for Healthcare Research and Quality maintains the National Guideline Clearinghouse website, a public resource for evidence-based clinical practice guidelines.

www.guideline.gov

Neuropsychiatric Inventory (NPI). The NPI screens for multiple types of dementia.

npitest.net

The Mount Sinai Conference on the Pharmacotherapy of Schizophrenia. This report provides guidance on the prescription and monitoring of antipsychotic medications, and it is available as a free full text download from Oxford Journals.

schizophreniabulletin.oxfordjournals.org/content/28/1/5.long

The Scottish Intercollegiate Guidelines Network (SIGN). SIGN 131, Management of Schizophrenia, provides a current set of guidelines on the evaluation and treatment of schizophrenia spectrum disorders as well as patient and family education materials.

www.sign.ac.uk/guidelines/fulltext/131/

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